DIABETIC RETINOPATHY IN END STAGE RENAL DISEASE OF TYPE–II DIABETES MELLITUS

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CHENNAI

Dept. Of Ophthalmology

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CERTIFICATE

This is to certify that this dissertation entitled "**DIABETIC RETINOPATHY IN END STAGE RENAL DISEASE OF TYPE -II DIABETES MELLITUS**" has been done under my guidance in Department of OPHTHALMOLOGY, MADURAI MEDICAL COLLEGE, MADURAI.

I Certify regarding the authenticity of the work done to prepare this dissertation.

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DECLARATION

I, **Dr. P. SARAVANA SANKAR**, Solemnly declare that the dissertation titled, "**DIABETIC RETINOPATHY IN END STAGE RENAL DISEASE OF TYPE -II DIABETES MELLITUS"** has been prepared by me.

This is submitted to the "**THE TAMILNADU DR.M.G.R.MEDICAL UNIVERSITY, CHENNAI**, In partial fulfillment of the requirement for the award of M.S., (Ophthalmology) Branch-III degree examination to be held in **APRIL 2012**

Place: Madurai

Date: **Dr. P. SARAVANA SANKAR**

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Last but not the least, I thank “God the Almighty”, for being my guiding light all the way.

CONTENTS

TITLE

INTRODUCTION

Eye is a mirror that reflects pathological changes occurring in many organs of the body. Numerous systemic disorders affect both eye and kidney. Examination of eye is an in dispensable part of the clinical assessment of a patient with renal disorders.

CRF is irreversible and progressive process that result in END STAGE RENAL DISEASE(ESRD) where patient has to depend on renal replacement for survival.[1]

Richard bright in 1836 first associated renal disease with blindness.[2] By ESRD 80% of pts will have secondary hypertension.[3] Ocular morbidity may be due to coexisting risk factors like hypertension, diabetes, uremia and anemia. The ophthalmologist may be consulted for a variety of reasons about the patients whose problem appear renal.

On the other hand nephrologists may be aware of many ocular manifestations of renal disorders which are common and rare in nephrology and the potential toxicity of therapeutic agents.

Inflammatory reactions of conjunctiva and episclera can be associated with sudden marked raise in serum calcium.[4 - 5] Conjunctival degenerative changes (e.g) pinguecula are frequently seen in CRF.[6]

Diabetes is the most common disorder with ocular and renal manifestations.[7] Rubeosis iridis and neovascular glaucoma occur due to posterior segment pathology. Rising concentration of intracellular calcium might contribute to early cataractegenesis and calcium deposit in lens.[8]

Hypertension affects the eye and kidney in parallel and very often occurs along with diabetes.

Hypertensive changes are particularly severe in renal failure. This has been attributed to the effects of retained nitrogenous products.[9] Accelerated Hypertension can result in optic disc edema.[10]

Renal disease and ocular complications in diabetes are frequently disturbing and destined to become one of the challenging problems of the future.

Blindness due to proliferative retinopathy or maculopathy is approximately 5 times in diabetic patients with nephropathy compared with non albuminuric patients.[11]In India majority of end stage renal disease patients are of type II diabetes . 5% of diabetic patients die of end stage renal disease.

Diabetic retinopathy (DR) tends to deteriorate with falling renal function and poorly controlled blood pressure.[12] Diabetic Microangiopathy

has been recognized as a major cause of kidney involvement in diabetes. Diabetic nephropathy ultimately leads to end stage renal disease.

Both anterior and posterior optic neuropathy can occur in CRF, when hemoglobin level falls below 5gm% retinopathic features like retinal hemorrhages, hard and soft exudates and pallor of optic discs could be present .The retinal arterioles look pale and veins appear distended.

Retinopathy is often asymptomatic in its most treatable stage. Delay in diagnosis can result in significant increase in patients risk of visual loss. Type II DM accounts for 90% - 95% diabetes cases and differs from type I diabetes in average age of onset and Etiology. [13]

Patients with type I diabetes, who are generally younger and are more likely to live long enough to benefit from tight glycemic control, than patients with type II disease, who face a shorter life expectancy, because of their age and risk of cardiovascular disease.[14] For patients with co-existent disease, the delayed benefits of glycemic control may be offset by the more immediate inconvenience, complications, and costs of intensive treatment and by the health effects of co morbid conditions. Ocular condition is also an indicator of metabolic control of the disease process.

Similarly an unknown case of chronic renal failure with its ocular complications, may first present to an ophthalmologist. This study is an

attempt to access the ocular status, complications associated with CRF. It is intended to highlight the importance of ocular examination, to screen patients for any potential visual threat, so that necessary treatment or advice can be given, before they become irreversibly visually impaired.

AIMS AND OBJECTIVES

a. To record the stage of retinopathy in end stage renal disease patients of diabetic origin and on treatment.

b. To record the progress of retinopathy at end of 6months and 12months in these patients.

c. To correlate the severity of retinopathy with renal failure.

d. To know associated findings with patients with diabetic retinopathy and diabetic nephropathy.

DIABETES – RENAL FAILURE – EYE

Diabetes is defined as a major group of metabolic disease characterized by hyperglycemia, with disturbances in carbohydrate, fat and protein metabolism either due to defect in insulin secretion, action or both.[15] It is the chronic hyperglycemia that causes most of the microvascular damage and contributes to the development of macrovascular disease.

In type I diabetes onset is symptomatic and after ten years seventy percent of the patients have retinal abnormalities and after twenty years 30-40% have clinical nephropathy. In type II diabetes the intial onset is asymptomatic and 15-20% have retinal abnormalities and 5-10% have sustained microalbuminurea at the time of diagnosis.[16]

MICROVASCULAR COMPLICATIONS

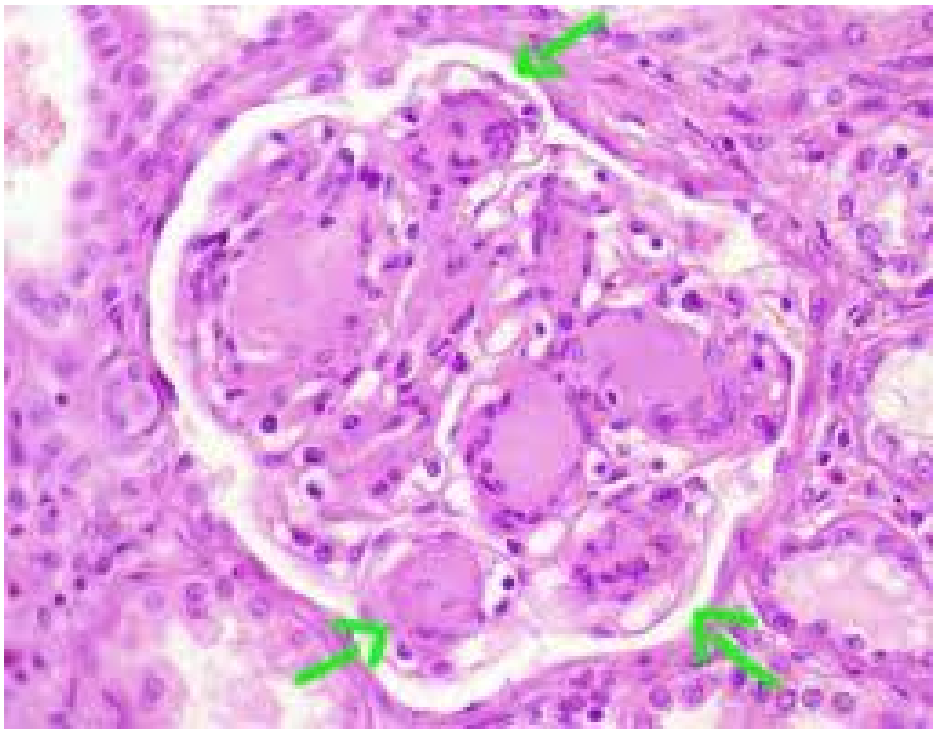
Nephropathy Retinopathy

Neuropathy

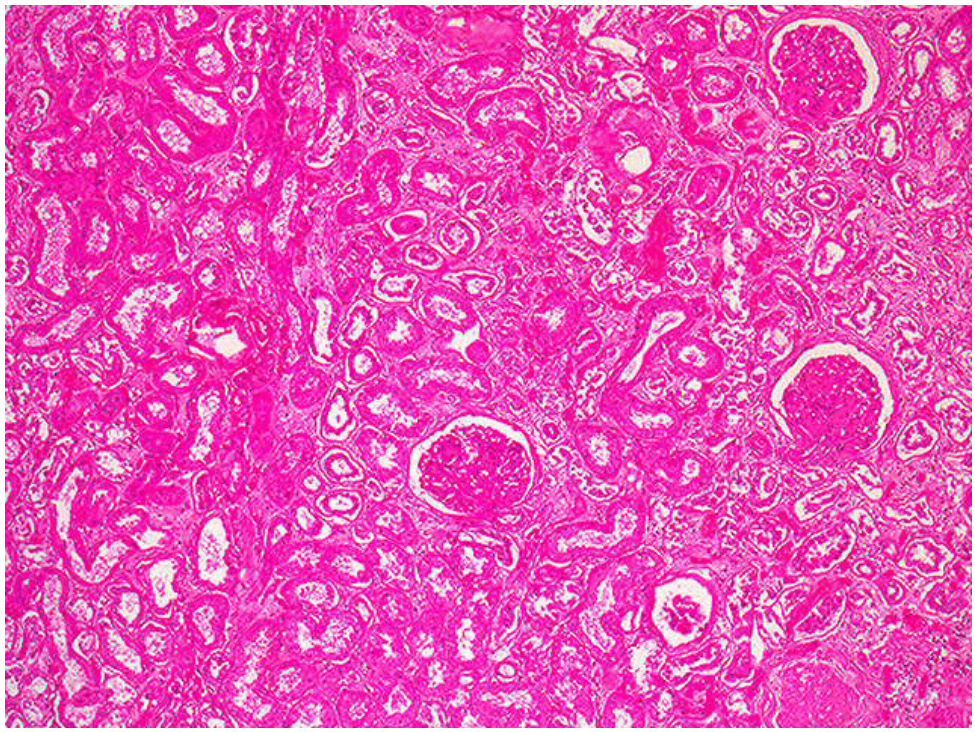
Macrovascular Complications

Accelerated and premature atherosclerosis involving cornea, cardiovascular and renal systems.

KIMMELSTIEL – WILSON LESIONS



PATHOLOGY PICTURE - 1



PATHOLOGY PICTURE - 2

Diabetic Nephropathy

The most frequent cause of renal involvement in disease affecting other organs is diabetes. Renal failure in those with Insulin dependent diabetes mellitus and disease duration of 5 years together with hypertension and retinopathy is highly suspicious of diabetic nephropathy.

In Non Insulin dependent diabetes renal involvement seems to occur as frequent as individuals with insulin dependent diabetes after the same duration of disease but in this age group other renal disease are common.

The kidney may be damaged in three ways[16]

1. Glomerular damage
2. Ascending infections
3. Ischemia due to hypertrophy of afferent and efferent arterioles.

DIABETIC GLOMERULAR SCLEROSIS

Clinical nephropathy secondary to glomerular damage usually manifests 15-25 years after the diagnosis and affects (30-40%) of the patients diagonised under the age of 30years.

It is the leading cause of premature death in young diabetic patients. Older diabetics develop nephropathy but the proportion affective is much smaller. The intial structural lesion in the glomerulus is thickening of the basement membrane. Associated changes may result in disruption of protein cross linkages that make the membrane an effective filter. In consequence a progressive leak of protein into the urine occurs.

The earliest evidence of this is microalbuminuria which in turn in some years progressed to intermittent albuminuria followed by persistent proteinuria. Once overt proteinuria occurs renal function invariably declines with 50% of the people reaching end stage renal disease with in 7 years of onset of proteinuria.

CHRONIC RENAL FAILURE

CRF is defined as permanent and significant reduction in glomerular filteration rate. In nearly all patients once GFR is reduced to 1/3rd of normal (below 30-40ml), Serum creatinine more than 8mg /1dl progressive renal failure develops and eventually leads to but often slowly and over the years to ureamic syndrome and end stage renal disease. Uraemia can be defined as sign's and symptoms associated with retention of end products of protein metabolism. The ureamic syndrome is quite variable and unpredictable in the time of onset during the course of renal failure

More commonly it occurs at blood urea nitrogen level of more than 100mg / dl and serum creatinine level of more than 10mg/ dl. It is good medical practice to initiate replacement theraphy just before the onset of ureamic symptoms usually when GFR is 5-10ml/ dl minute.

END-STAGE RENAL DISEASE

ESRD is final common end despite the dissappearance of renal insult that initially lead to the loss of some nephrons. It is striking that 60% of ESRD is now due to diabetes and essential hypertension. The most common primary renal cause of failure is glomerulo nephritis.

MANAGEMENT

The under lying cause of renal disease should be treated aggressively wherever possible eg. Tight diabetic control.

The Guideline of treatment are :

- Blood pressure control
- Treatment of hyperkalemia
- Correction of acidosis
- Regular treatment of hypocalcemia and hyperphosphatemia.
- Dietry protein restriction

- Fluid restriction along with salt.
- Treatment of hyperlipedemia
- Correction of aneamia
- Patient education

RENAL REPLACEMENT THERAPY

- Haemodialysis
- Haemofiltration
- Haemodiafiltration
- Peritoneal dialysis
- Kidney transplantation

When no contraindication exists, all patients received renal replacement therapy. Initially patients with ESRD are managed by conservative therapy but eventually they required haemodialysis, Peritoneal dialysis or transplantation. Because of limited success of each of these modalities ESRD should be approached with the concept of moving from one form of therapy to another.

DIALYSIS IN ESRD OF DIABETES MELLITUS

No distinction is attempted in ESRD treatment outcome between type I and type II diabetes mellitus patients. Today it is generally accepted that the renal replacement therapy should be considered earlier in diabetic than non-diabetic ureamic patients.

Except in severe macroangiopathy, renal transplantation should be the first objective. Today an increasing proportion of patients who are accepted for the renal replacement therapy have diabetes and suffer from retinopathy. It is therefore essential that the nephrologist is familiar with the principles of treatment and major complications of the disease particularly retinopathy, diabetic foot and cardiac problems which are the main causes of morbidity and mortality.

CLASSIFICATION OF DIABETIC RETINOPATHY

- Duke – Elder
- Airlic – House

This system proposes fundus photography, flourescein angiography, ophthalmoscopy, fundus diagrams and slit lamp biomicroscopy of the retina.

- **Kanski Classification**

This is the popular and widely accepted classification of diabetic retinopathy. It is basically treatment oriented ophthalmoscopic classification.

- **Modern ETDRS Classification**[17,18]

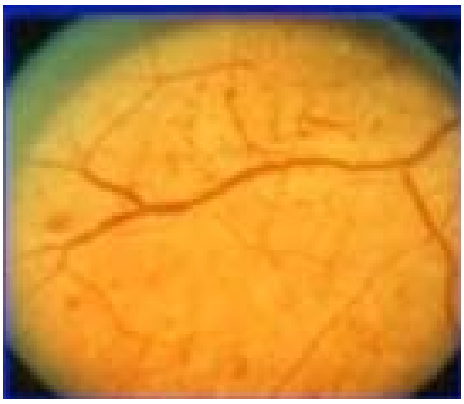
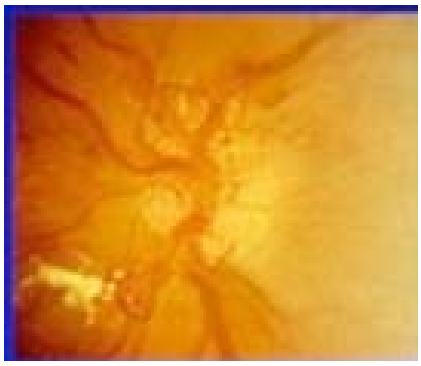
The early treatment diabetic retinopathy study has developed systems to grade the severity of diabetic retinopathy at various stages by assessing the lesions seen through stereoscopic colour fundus photographs and fluorescein angiograms.

NON-PROLIFERATIVE DIABETIC RETINOPATHY

A.MILD NPDR

At least one microaneurysm. Definition not met with B, C, D, E, and F.

DIABETIC RETINOPATHY DISEASE SEVERITY SCALE

<table>
<tr>
<td>Mild NPDR
 
Microaneurysms only</td>
<td>Moderate NPDR
 
More than just Microaneurysms but less than severe nonproliferative diabetic retinopathy</td>
</tr>
<tr>
<td>Sereve NPDR
 
Any of the following
➢ 20 intraretinal hemorrhages in each of 4 quadradants OR
➢ Definite venus beading in 2+ quadrants OR
➢ Prominent IRMA in 1+ quadrant and no PDR</td>
<td>Proliferative DR (PDR)
 
1 or more of
➢ Neovascularization
➢ Vitreous/ preretinal hemorrhage</td>
</tr>
</table>

B. MODERATE NPDR

Hemorrhages and/or microaneurysm- standard photograph 2A and / or soft exudates, venous beading or IRMAs definitely present. Definitions not met with C, D, E and F.

C. Severe NPDR

Hemorrhages and/or microaneurysms in all four quadrants. Venous beading in two or more quadrants. IRMA>Standard photograph # 8A in atleast one quadrant.

D. Very Severe NPDR

Any two or of C.

Definition not met with E,F.

PROLIFERATIVE DIABETIC RETINOPATHY

E. EARLY PDR

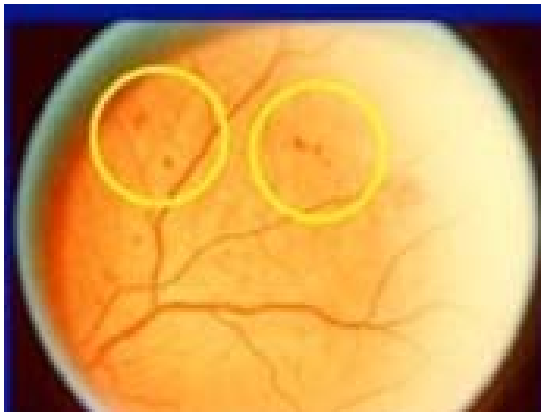
New vessels.

F. HIGH RISK PDR

NVD 1/3- ½ disc area or

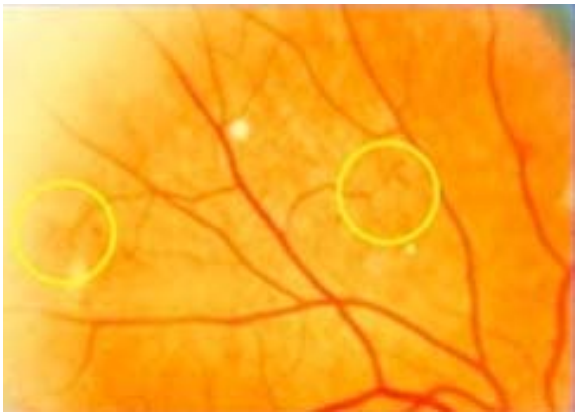
NVD & Viterous/preretinal

4-2-1 Rule



4 quadrants H/MA (STD 2A)

4 quadrants VB



1 quadrant IRMA (STD 8A)

Any of these situations – SEVERE NPDR

NVE – ½ disc area and preretinal/vitreous hemorrhage

In retina, the primary sources VEGF – A are ganglion cells. Muller and colleagues have shown that the level of VEGF (A) –in ocular tissues correlates with new vessel formation [19].

PROLIFERATIVE DIABETIC RETINOPATHY

The exact pathogenesis of retinal neovascularization remains unclear. In 1948, observations led Michelsen to propose that there exists in the retina a risk factor or factors affecting the budding of new vessals. Later it was explained by Ashton and others that hypoxia was the primary stimulus for production of angiogenic factors.

The most frequently studied molecules include basic fibroblast growth factor (bfgf), vascular endothelial growth factor (VEGF) growth hormone, and more recently the angiopoietiens studies however indicate VEGF as the main predictor of angiogenesis.[20,32,33]

EPIDEMIOLOGY OF DIABETIC RETINOPATHY

The Wisconsin Epidemiologic[15,30] study of diabetic retinopathy was a large population based study on subjects with diabetes with younger onset and those diabetics after 30 years. Few important results were,

NEO VASCULARISATION AT DISC (NVD)

NEO VASCULARISATION ELSEWHERE (NVE)

- Severity of retinopathy was related to the duration of diabetes ranging from 2% in subjects with diabetes for less than 2yrs to 98percent in subjects with diabetes for 15yrs or more[32]. The severity also increased with duration of diabetes.

- In contrast the older onset was likely to have retinopathy at the time diabetes was diagnosed.

The study also found out that elevated glycoslylated hemoglobin was associated with severe retinopathy in all age groups. Proterniuria was associated with severe retinopathy in both groups.

PROLIFERATIVE DIABETIC RETINOPATHY

NVD

Neovascularization is frequently found within 45degrees of the optic disc. It is observed at the disc as a cart wheel configuration radiating from the center best indentified by stereoscopic view, by either contact or precorneal lenses or stereoscopic photography.

NVE

All other neovscularization other than from disc is called NVE. it occurs typically adjacent to areas of capillary closure, marked by cotton

wool spots and hemorrhagic microaneurysms. IRMA may be difficult to differentiate from early NVE. Flourescein angiography shows leakage in new vessels as a differentiating feature.

VITREOUS AND PRERETINAL HEMORRHAGE

Small hemorrhages may occur near growing tips of the vessel but they are usually subhyaloid. Progression of vitreous detachment starts on either side of vascular arcades of fovea. Vitreous usually remains attached to the disc by proliferating fibrovascular tissue. Vitreous hemorrhage may occur as a result of vitreous traction on new vessels.

VITREOUS TRACTION AND FIBROUS PROLIFERATION

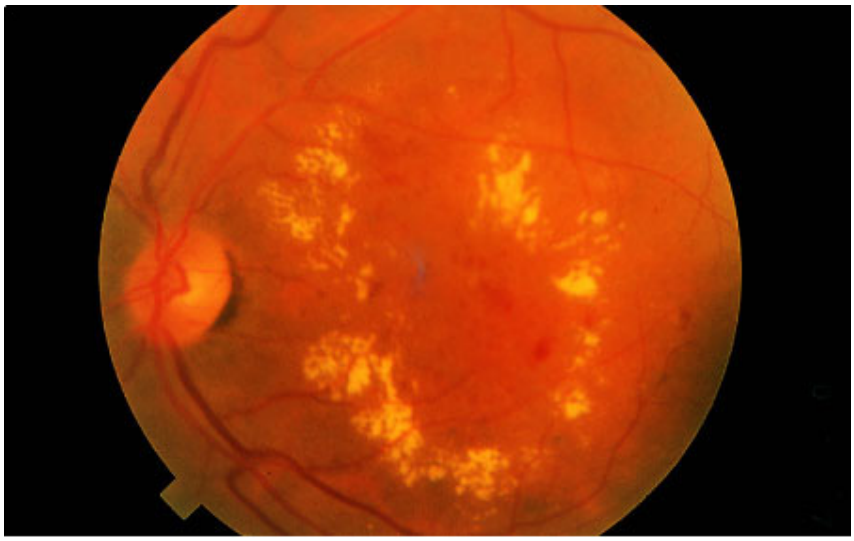
Fibrous tissue develops along the vessels which may subsequently contract. Contraction of posterior vitreous face and fibrovascular proliferation leads to tractional retinal detachment. Retina along the temporal arcades is the first to detach and extends to involve the fovea. Contraction of fibrovascular tissue can also lead to distortion or horizontal displacement of macula.

RUBEOSIS

Iris neovascularization in diabetes is observed in proliferation changes and also in long standing changes of diabetic retinal detachment.

HYPERTENSIVE RETINOPATHY

CLINICALLY SIGNIFICANT MACULAR EDEMA



DIABETIC MACULOPATHY

Diabetic macular edema may be present at any level of retinopathy and alters the structure of macula in any of these manners.[21]

- Macular edema, i.e., a collection of intraretinal fluid in the macula with or without lipid exudates and with or without cystoid changes
- Non perfusion of parafoveal capillaries with or without intraretinal fluid
- Traction in the macula by fibrous tissue proliferation causing surface wrinkling or macular detachment
- Intraretinal or preretinal hemorrhage in the macula
- Lamellar or full thickness retinal hole formation
- Any combination of the preceding.

CSME as defined by ETDRS includes any of these

- Retinal thickening at or within 500microns of the center of macula
- Hard exudate at or within 500microns of the center of the macula, if there is the thickening of the adjacent retina
- Any are of retinal thickening at least one disc area in size at least part of which is within 1 disc diameter of the center of the macula.

REVIEW OF LITERATURE

OCULAR COMPLICATIONS OF RENAL FAILURE

The association of blindness and end stage renal disease was first noted by Bright and fundus changes in uraemic patients was described by Leibrich.[21,22,23] Subsequently this was named Bright disease or albuminuric retinitis. By the end of the nineteeth century and as a result of hypertensive changes, albuminuric was no longer consider as a separate entity, but as manifestation of hypertension in uraemic patients.

Since the introduction of effective anti hypertensive treatment, dialysis and kidney transplantation such patients with severe hypertension have become rare. Never the less hypertension is still an important problem in kidney diseases and complications of atherosclerosis is common in renal patients as a result of chronic hypertension and hyperlipidaemia.

VASCULAR LESIONS

Arterial hypertension is a frequent complication of a congenital and acquired renal and renovascular disorders. Arteriolar narrowing, tortuosity occur in patients with severe hypertension and ischemic changes may occur in retina, choroids and optic nerve producing cotton wool spots, hard exudates, exudative detachments, disc edema and optic atrophy.

BLINDNESS

In patients with severe and long standing hypertension a severe reduction in arterial pressure may cause infarction of optic nerve followed by blindness or visual loss. In occasional patients with cerebrocortical infarction occurs under these circumstances with cerebral blindness. Anterior ischemic optic neuropathy and retinal infarction have been described as complication of haemodialysis associated with hypotension. Uraemia, anemia and disc edema due to intracranial hypertension are other risk factors for optic neuropathy in patients with renal disease. In addition patients with chronic hypertension are predisposed to retinal arterial and venous obstructive disease leading to visual loss. Sudden blindness like purtschners like retinopathy with or without cotton wool spots may occur in patients in chronic renal failure with or without trauma, pancreatitis or autoimmune disease. The precipitating factors for this retinovaso-occlusive disorder remain unclear. The conditions have been described in renal transplant also.

SEROUS RETINAL DETACHMENT AND CORTICOSTEROID INDUCED CHANGES IN RETINAL PIGMENT EPITHELIUM

Serous retinal detachment and diffuse retinal pigment epitheliopathy or chronic central serous chorioretinopathy may follow organ

transplantation, haemodialysis or patients receiving steroid therapy. In severe forms bilateral bullous retinal detachment, multiple retinal pigment epithelial detachments and yellow fibrin like subneural exudates beneath the sensory retinal detachment may be observed.

Flourescein angiography shows wide spread retinal pigment epithelial changes and leakage's. Several factors may play a role in precipitating serous detachment in patients with renal failure, including impaired fluid and electrolyte imbalance, choroidopathy associated with hypertension, thrombotic microangiopathy or immune complex vasculitiditis and dysfunction of overlying epithelium which may be associated with renal disease such as membranoproliferative glomerulonephritis type 2. Corticosteroid can damage the RPE and predispose a patient to serous retinal detachment. Where as stress may produce chronic serous retinopathy. The visual prognosis is unfavourable. A decrease of corticosteroid dosage may help in reducing visual symptoms and enhance resolution of retinal detachment. In refractory cases focal laser photocoagulation may be applied to leakage points.

GLAUCOMA

Intraocular pressure may increase during haemodialysis and cause acute angle closure glaucoma in predisposed patients with increased

resistance to aqueous outflow. The increase in pressure is thought to be part of cerebral edema that occurs as a consequence of the rapid reduction in serum osmolality. Corticosteroid is another risk factor for an increased intraocular pressure. In patients who are beginning long term haemodialysis or corticosteroids intraocular pressure should be measured early as diagnosis and treatment of glaucoma may prevent visual loss.

CORNEAL CALCIFICATION IN RENAL FAILURE

In patients with renal failure and associated hyperparathyroidism soft tissue calcification are first detected first in the peripheral interpalpebral cornea and adjacent conjunctiva. The corneal calcification eventually spread to toward visual axis in patients on chronic intermittent haemodialysis producing band keratopathy with decrease in visual acuity epithelial erosions resulting in severe pain. Patients with renal failure and hypercalcemia may present with inflamed pingecula and diffuse inflammatory edema.

BROWN TUMORS OF THE ORBIT

Brown tumors of the orbit are observed with the renal failure and secondary hyperparathyroidism. Brown tumors are focal bony lesions composed of giant cell masses and extravasation of blood affecting patients with primary or secondary hyperparathyroidism.

DIABETIC RETINOPATHY AND RENAL FAILURE

Nephropathy and retinopathy are the major microvascular complications of diabetes.[22,23] It is the chronic hyperglycemia that cause most of the microvascular damage and contributes to the development of the macrovascular disease. This microangiopathy affects nearly all diabetics and while most diabetics and while most diabetics may develop clinically evident retinopathy, nephropathy occurs in a subset.

In patients with nephropathy retinopathy is always present and proliferative retinopathy is common. However thirty five percent of the patients with proliferative retinopathy have no signs of diabetic nephropathy and these patients will probably never develop diabetic nephropathy.

Retinopathy tends to deteoriate as renal failure develops in patients with poorly controlled blood pressure and in patients in whom no treatment has been given. In WESDR study proteinuria was strongly associated with diabetic retinopathy. Older onset diabetes with proteinuria were also more likely to have proliferative retinopathy. Renal retinopathy will overlie diabetic retinopathy and consist of a hypertensive component and a ureamic component. The hypertensive changes include nerve fibre layer infarcts, cotton wool spots and arterio-venous changes. The Ureamic changes include

disc edema and diffuse macular edema which may lead to massive macular edema.

Macular edema, glaucoma, cataracts and corneal diseases must be considered in diabetics facing blindness. Preservation of vision correlates well with blood pressure control and that patients with end stage renal disease suffering from diabetes now enjoy an equivalent visual prognosis whether treated by dialysis or undergo renal transplantation. It is important to consider laser photocoagulation for proliferative or pre-proliferative diabetic patients facing renal failure.

Since the progression of diabetic retinopathy is independent of diabetic nephropathy and not reversed by treatment of nephropathy, further follow up and treatment of diabetic retinopathy is imperative. In the past visual prognosis in dialysed diabetics was extremely poor(according to Shapero and County 1980), beginning dialysis between 1966 and 1971 had twenty nine percent risk of becoming blind and vision was lost in forty one percent in eyes at risk. These figures have improved in parallel with improvement in dialysis procedure and better control in blood pressure. Patients admitted between 1976 and 1979 had only one percent risk of amaurosis on dialysis. This observation invalidates past concerns that administration of heparin during dialysis adversely affects visual prognosis. Clear evidence documents that blindness in end stage renal disease is

avoidable. In addition, hypertension accelerates the evolution of background retinopathy to proliterative retinopathy. Treatment of hypertension and renal disease will decrease retinopathy particularly macular edema and stabilize vision.

Watnabe at all followed two hundred and sixty eight Japanese diabetic on haemodialysis who had fifty percent survival at six months with stable visual activity in three hundred and sixty four of four hundred and eighteen eyes 87.7% while twenty of the four hundred and eighteen eyes 8% deteoriated.

ROLE OF PHOTOCOAGULATION

Diabetic end stage renal disease patients with persistent macular edema may benefit from macular photocoagulation. In diabetics with active proliferative retinopathy, pan retinal photocoagulation,[22,27] may improve the visual prognosis by inducing involutional retinopathy and by removing vitreous hemorrhage and viteroretinal tractions. More over diabetes with end stage renal disease are predisposed to cataracts which may require surgical intervention. The progress made in improving the visual prognosis in diabetic end stage renal disease reflects the synergistic efforts made by physicians and ophthalmologists and emphasize the importance of team approach in preventing blindness.

DIABETIC RETINOPATHY AND RISK FACTORS

Approximately 10% of diabetic population has type I (Insulin dependent) diabetes mellitus which is usually diagnosed before the age of forty years.[31] The majority of diabetic patients, however have a type II (non insulin dependent) diabetes mellitus which is usually diagnosed at the age of forty years. These patients may or may not be treated with insulin.

Although these patients with type I diabetes mellitus experience a high incidence of severe ocular complications and are more likely to have significant ocular problems during their life times, those with type II diabetes mellitus make up the majority of the clinical patients with the diabetic eye disease.

RISK INDICATIONS OF RETINOPATHY

JOINT CONTRACTURE

Association of retinopathy with contractures has been established. Eye examination in cases of joint contracture is needed.

NEUROPATHY

Neuropathy in lower extremities may alter mobility in such a way that restoration maintenance of as much vision as possible is important.

Cardiovascular autonomic neuropathy is an independent risk factor for proliferative diabetic retinopathy.

CONDITIONS THAT MAY AFFECT THE COURSE OF DIABETIC RETINOPATHY

HYPERTENSION

Appropriate medical treatment is indicated for prevention of cardiovascular disease, stroke and death. Hypertension itself may result in hypertensive retinopathy super imposed on diabetic retinopathy.

ELEVATED TRIGLYCERIDES

Appropriate management is important. Proper diet and reduced levels may result in less retinal vascular leakage.

PROTEINURIA

Aggressive management of elevated creatnine in renal disease is indicated to avoid renal retinopathy which may increase the risk of progression of diabetic retinopathy.

CARDIOVASCULAR DISEASE

Increased risk of cardiovascular disease particularly coronary vascular disease if often associated with an increased attenuation and atherosclerotic

closure of arterial system of retina.[29] A decreased risk of hemorrhage into the vitreous may result but they may also be decrease in retinal function with an associated decrease in vision. Management of cardiovascular disease may help relieve some of the ischemic process in retina.

CLINICAL TRIALS

There are no clinical trials that have specifically shown that control of systemic conditions that may affect the eyes, prevents the progression of diabetic retinopathy. Clinical experiences suggest an association with the systemic benefits of appropriate treatment of these problems.

- Effect of haemodialysis on diabetic macular leakage. Tokuyama T, Ikeda T, Satok[26]

Aim

To evaluate the effects of haemodialysis on macular oedema by flourescein angiography in patients with diabetic retinopathy and end stage renal disease.

Results

Flourescein angiograms obtained at 4 weeks showed that macular leakage was unchanged (70%), decreased in 10% and increased in 20% when compared with the basic line appearance.

Conclusions

These results indicate that haemodialysis does not benefit macular leakage in diabetic patients receiving haemodialysis for end stage renal disease.

- Renal pathology patterns in type II diabetes mellitus:relationship with retinopathy. The collaborative study group. (Schwartzmann, Lewis EJ, Leon, Martin T , Lewis JB, Battle D.)

Background

The glomerular and retinal vessels and are both affected in patients with type I and type II diabetes mellitus. However, the prevalence of nodular form of diabetic glomerular sclerosis (Kimmelstiel/Wilson lesion) and other forms of glomerular pathology including diffuse mesangial sclerosis and their clinical correlates in type II are less well known.

Results

Patients with Kimmelestial Wilson nodules had more severe overall retinopathy than those with mesanglial sclerosis lesion. Six of seven with proliferative retinopathy had kimmelstiel Wilson nodules and seven without retinopathy had mesanglial sclerosis lesions.

- A co-relation of the eye and kidney in diabetes mellitus and hypertension. Yazdani I, Ahmed S, Channa A, Gayoori.
- The study was undertaken to observe the co-relation between microangiopathic changes in diabetic retinopathy and microvascular changes in diabetic nephropathy. Included in the study were 64 patients with chronic renal failure who were on maintenance dialysis, 40had hypertension alone, 21 hypertension and diabetes and 3 had diabetes alone. On examination of retina, of 40 hypertensive patients, 14 had positive findings, while in the hypertensive and diabetic and diabetic group, 20Patients out of 21, had positive findings. Nine patients in the hypertensive group had delayed chorodal filling on fluorescein angiography which was not very accurately reflected on funduscopy. In the diabetic and hypertensive group, 13patients having proteinuria of more than 1gm, also had exudates and haemorrhages in

the fundus. It was concluded that a correlation exists between the arterial changes in the fundus of the eye and the glomeruli of the kidney.

- Clinical and epidemiological aspects of diabetic retinopathy and its relationship with diabetic nephropathy.

Ergrafov Vlu, Mamaeva, Bishele NA, Luidina LI. Results of clinical and laboratory examinations of 161 diabetes are presented. The main factors or risk of nonproliferative diabetic retinopathy are the duration and degree of compensation of diabetes mellitus, development and stage of diabetic nephropathy, the latter factor replacing in experiments with simulation of diabetic retinopathy the level of arterial hypertension, and the blood serum content of high-density lipoprotein cholesterol and ration of total cholesterol to high- density lipoprotein cholesterol.

- Discordance between retinopathy and nephropathy in type 2 diabetes KanauchiM, Kawano T, Uyamo H, Shiki H, Dohi K.

A total of 22 Patients with type 2 diabetes (139 males and 82 females) who consecutively underwent renal biopsy between 1982 and 1996 were investigated. The severity of diffuse glomerular lesions was graded using the criteria a Gellman and coworkers, and diabetic retinopathy was classified

as absent, nonproliferative, or proliferative. The incidence of advanced nephropathy without retinopathy for all 22 cases with 2.3%.

- Retinal complications in diabetics with renal failure DufierJL, Nguyen HV, Funck- Brentano JL

Study concluded on a series of 27 patients that all diabetics with end stage renal failure had retinopathy excepting one. Retinopathy, its severity and the prevalence of complications are primarily related to the evolution of diabetes, whatever the type and severity of the nephropathy. The aim of the study was to investigate the relationship between the grade of retinopathy and the severity of glomerular lesions in patients with type 2 diabetes. Results: only 5 patients of the 221 cases had no retinopathy. The rest of the cases either had absent, nonproliferative or proliferative retinopathy. The findings of this study were consistent with the hypothesis that there are important differences in some aspects of the pathogenesis or retinopathy and nephropathy.

- Proliferating retinopathy in diabetes mellitus. Clinincal and autopsy results. Fishcher F.

Clinical and autopic investigations of thirty patients suffering from diabetes mellitus and retinopathia proliferans result in the findings that of the

various manifestations only retinopathy, nephropathy, and arterial hypertension are present in all cases, all other forms receding into the background. Conclusion : Diabetes mellitus in connection with retinopathia proliferans turns out to be the most serious form of the general diabetic disease.

- Clinical profile of Indian non-insulin – dependent diabetics with nephropathy and renal failure. John L, Ganesh A, John G, Raju JM, Kirubakaran MG, Shastry JC.

Study conducted on 296 non-insulin depend and diabetic NIDDM Patients with nephropathy and renal failure. Results : Male preponderance was striking in this group and the age of onset of diabetes was between 30 and 50 years in 75%. Retinopathy was present in 86% with proliferative changes in 20% and coronary artery disease in 40% of the people. It was observed that people with NDDM developing nephropathy and renal failure had early onset of the disease and are significantly more male.

- Aggressive opthalmological management in diabetic end stage renal disease : A study of 31 consecutively referred patients: David H Berman, Eli A Friedman, Andrew P.Lurdin.

Prospective follow up of eye disease in patients with diabetic end stage nephropathy in referral unit of total 31 patients. Visual acuity and

diabetic retinopathy stabilized or improved in all 18eyes of the transplant patients and 41 of 44 eyes of the dialysis patients.

- Visual status in Diabetic patients following: Therapy for end-stage nephropathy.

Robert C.Ramsay, M.D., Herbert L.Cantrill, M.D.William H, Knobloch, M.D., Christina M, Comty, M.D.,[28]

One hundred sixty five renal transplant recipients and 43 patients on dialysis therapy for diabetic nephropathy were followed in a prospective study of visual function.[26] Visual acuity improved or remained stable in 74 percent of the transplant group and 58percent of the dialysis group. For both groups, visual deteriotion increases with duration of follow up and is related to the presence of active retinopathy. Renal transplant is the treatment of choice for diabetic nephropathy with regard to maintenance of visual function.

PART –II

MATERIALS AND METHODS

PATIENTS AND METHODOLOGY

This is a prospective non randomized study of 50 patients who were diagnosed end stage renal disease of diabetic etiology with or without hypertension. The onset of end stage renal disease was restricted to be less than six months.

The following criteria were to be noted to fulfil the diagnosis of ESRD

1. Raised BUN about 100mg/dl at time of diagnosis.
2. Raised serum creatinine about 8mg/dl.
3. Signs and symptoms of Uraemia for more than 3 months.
4. Known diabetic for more than 5yrs with retinopathy.
5. Only NIDDM patients were included.

Patients with underlying etiology other than diabetes and hypertension were rejected. Patients with concomitant eye disease were also rejected. Patients underwent regular hemodialysis of once a week. The type of dialysis

is bicarbonate and few patients underwent acetone dialysis. Where acidosis is present only bicarbonate dialysis is done.

OPTHALMOLOGICAL EXAMINATION

Opthalmological examination is made twice and whenever the patient reports with diminished vision.

Complete opthalmological evalution included

- Best corrected visual acuity.
- Slit lamp examination of both eyes.
- Direct opthalmoscopy.
- Fundus examination with 90D lens and slit lamp.
- Fundus photographs and FFA in suspicion of neovascularization.
- Diabetic retinopathy is classified as per ETDRS classification.
- Hypertensive retinopathy classified as per Keith Wagner Barker classification.

Table 1

OBSERVATION & ANALYSIS

AGE &

SEX DISTRIBUTION

TOTAL NO OF PATIENTS - 50

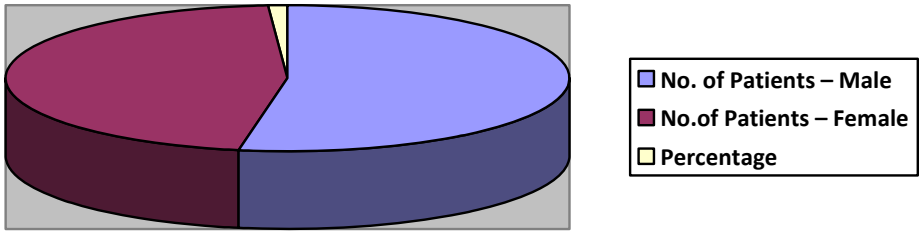
Age	No. of Patients – Male	Percentage	No.of Patients – Female	Percentage
55-60	16	32	14	28
61-65	2	4	8	16
66-75	4	8	6	12
Total	22	44	28	56

Majority of the patients in this study were screened within 6 months of the start of symptoms of uremia patients were already under taking treatment for diabetes mellitus other with oral hypoglycaemic agents or insulin.

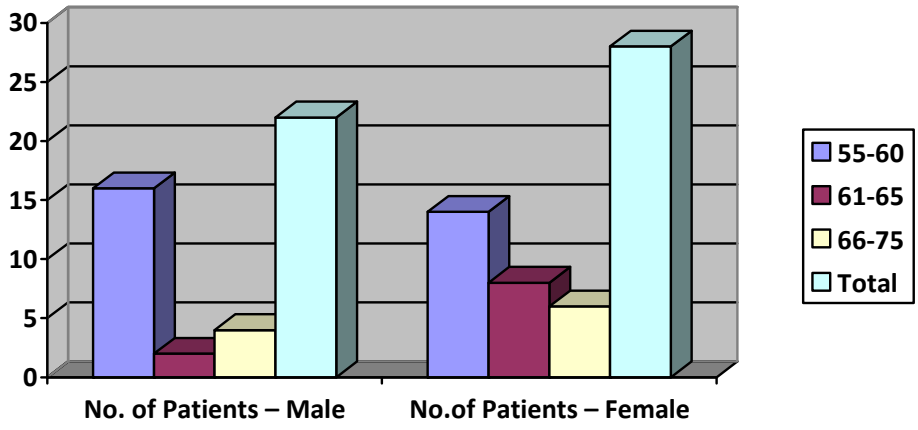
Majority of the patients were in the age group 55-60yrs, accounting to about 60%-men 32% & women 28%.

Most of the patients were women, accounting for 56% of the total.

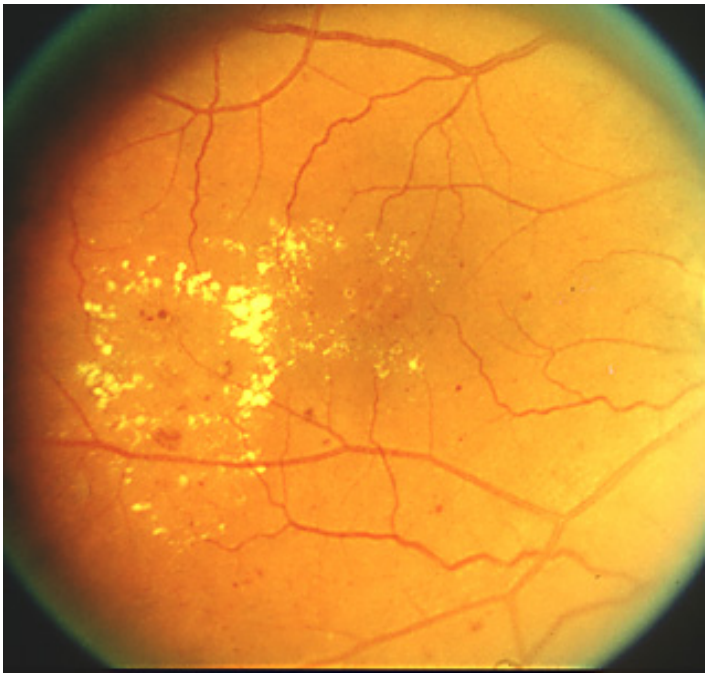
SEX DISTRIBUTION



AGE DISTRIBUTION



FUNDUS PICTURE OF JEYARAMAN – 55/ M – CASE- 1
(MODNPDR + CSME)



FUNDUS PICTURE OF CHINNASAMY – 57/ M – CASE- 4
(MODNPDR + GRADE 1 HTR CHANGES)

TABLE 2

DURATION OF DIABETES MELLITUS

IN RELATION TO ESRD

TOTAL NO OF PATIENTS -50

Duration of DM (Years)	No. of Patients
5-10	6
11-15	28
16-20	14
>20	2

Only NIDDM patients were taken in the study

All patients were known to be diabetic for more than five years.

Patients who were diabetic of about 11-15 years accounted for the majority.

Table 3

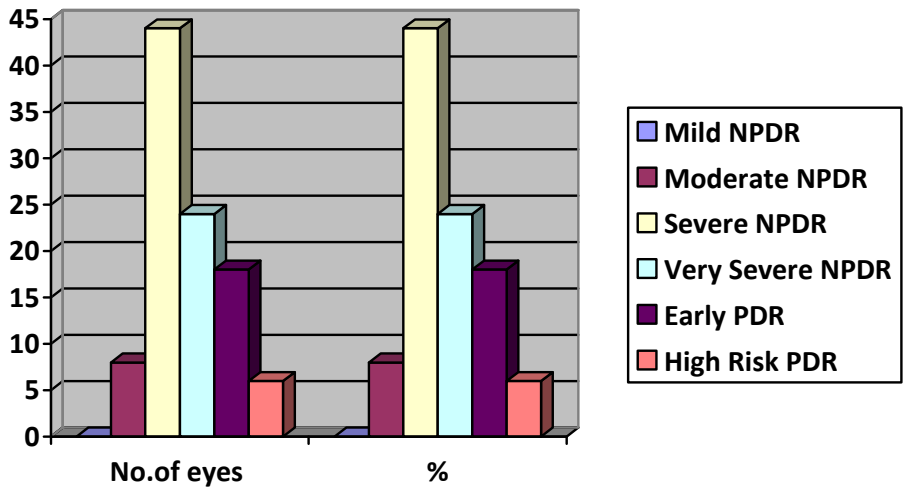
SEVERITY OF DIABETIC RETINOPATHY

AT BASELINE

TOTAL NO OF EYES = 100

Severity of Diabetic Retinopathy	**No.of eyes**	**%**
Mild NPDR	0	0
Moderate NPDR	8	8
Severe NPDR	44	44
Very Severe NPDR	24	24
Early PDR	18	18
High Risk PDR	6	6

SEVEIORITY OF RETINOPATHY 1



All patients of NIDDM with ESRD had retinopathy.

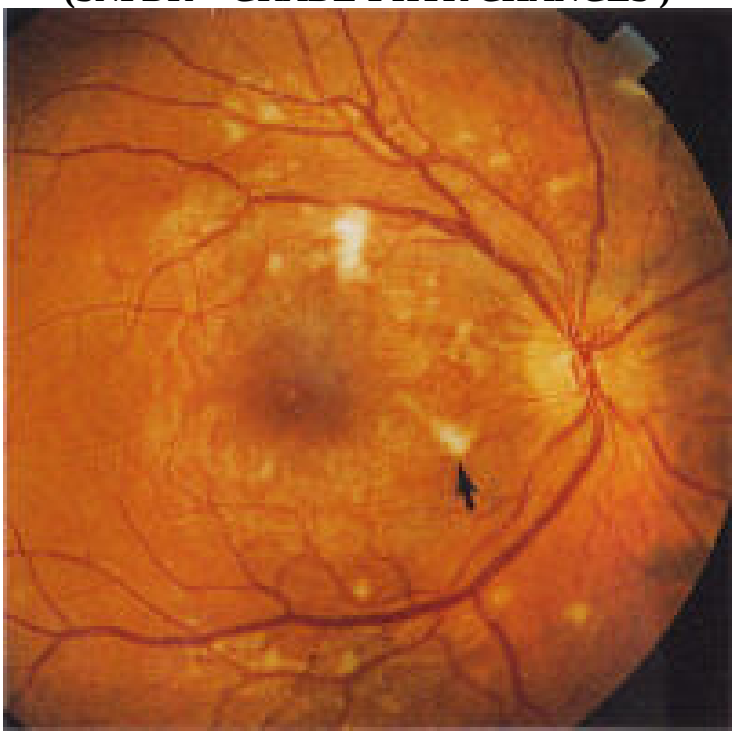
Diabetic Retinopathy is graded under ETDRS classification.

Non proliferative retinopathy in the form of severe retinopathy is the commonest retinopathy.

The distribution was mild NPDR ‘0’, moderate NPDR in 8% severe NPDR 44% , very severe NPDR 24%, early PDR 18% and high risk PDR 6%.

All patients underwent opthalmological examination with in one year of HAEMODIALYSIS and this was taken as base line retinopathy.

FUNDUS PICTURE OF LAKSHMANAN – 56/ M – CASE- 6
(SNPDR + GRADE 1 HTR CHANGES)



FUNDUS PICTURE OF RAMESH – 59/ M – CASE- 9
(SNPDR + CSME)

BASE LINE RETINOPATHY

FOLLOWUP RETINOPATHY

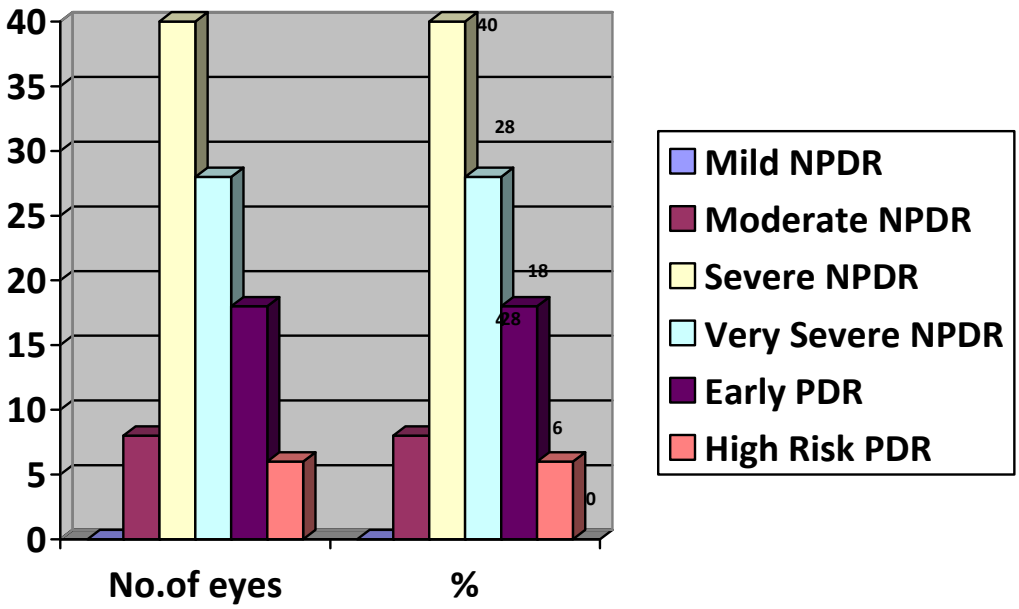
TABLE -4

SEVERITY OF DIABETIC RETINOPATHY

AT FOLLOW UP :

TOTAL NO OF EYES :100

Severity of Diabetic Retinopathy	No.of eyes	%
Mild NPDR	0	0
Moderate NPDR	8	8
Severe NPDR	40	40
Very Severe NPDR	28	28
Early PDR	18	18
High Risk PDR	6	6



Follow up examination of retinopathy was done at the end of 6 months and one year.

Majority of the eyes was found to be stable at the end of 6months and one year.

4 eyes with severe NPDR had progressed to very severe NPDR.

No new vitreous haemorrhage, or retinal detachment was noticed.

Table 5

CLINICALLY SIGNIFICANT MACULAR EDEMA IN DIALYSED ESRD AT BASELINE

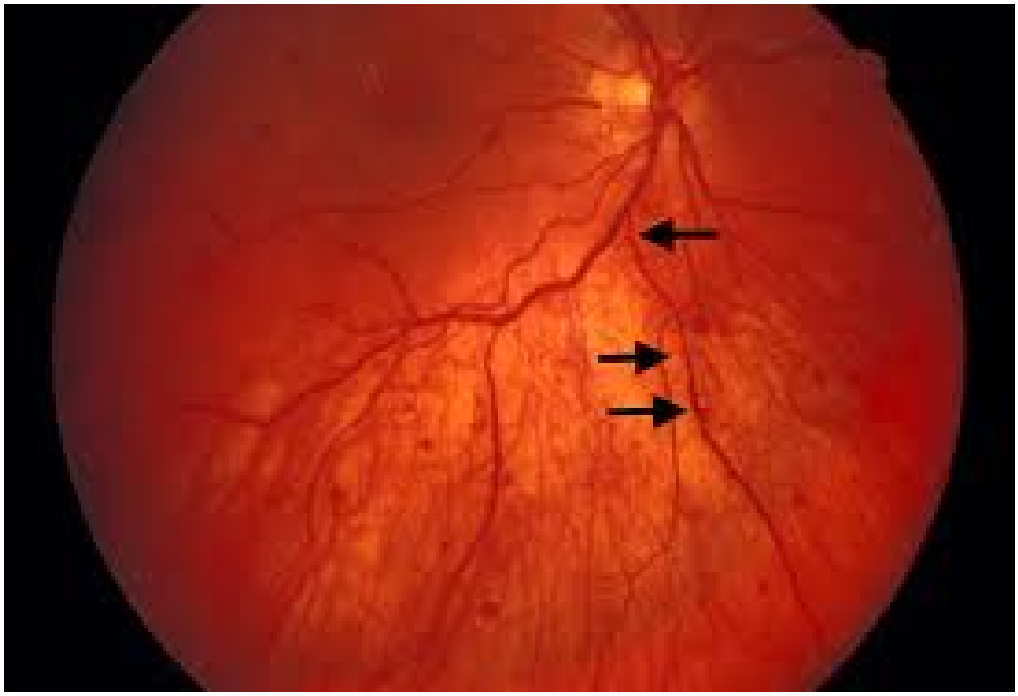
TOTAL NO OF EYES : 100

Severity of diabetic Retinopathy	No : Eyes	Percentage
Mild NPDR	0	0
Moderate NPDR	2	2
Severe NPDR	16	16
Very severe NPDR	6	6
Early PDR	7	7
High Risk PDR	0	0
Total	31	31%

CSME was noticed in 31eyes of the total.

Eyes with severe NPDR which accounted for majority also had the majority of CSME.

FUNDUS PICTURE OF VEILVENDAN -62 /F – CASE- 33
(VSNPDR)



FUNDUS PICTURE OF PANDI– 66/ M – CASE- 41
(EPDR + CSME)

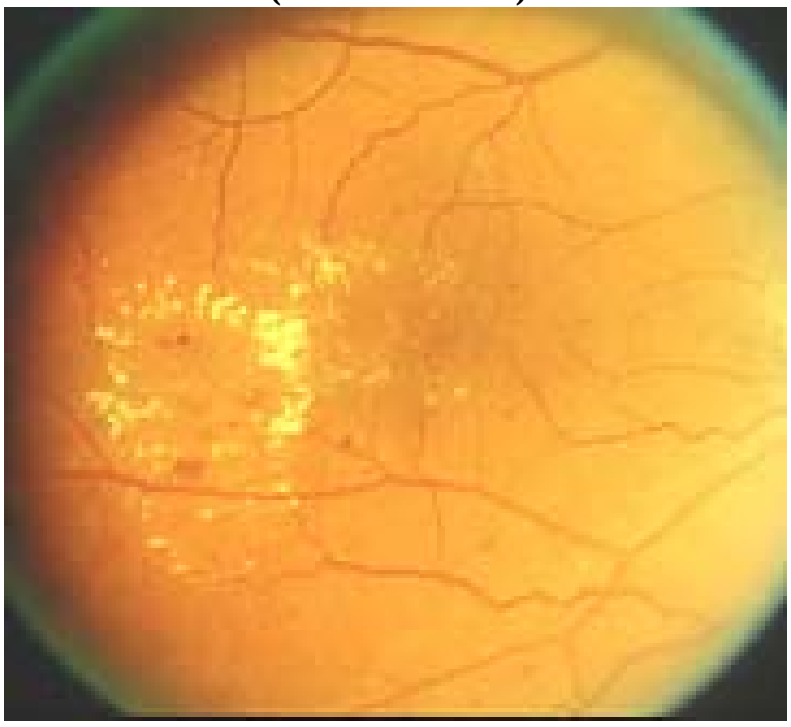


TABLE 6

CLINICALLY SIGNIFICANT MACULAR EDEMA IN DIALYSED DIABETIC ESRD AT FOLLOWUP

TOTAL NO. OF EYES = 100

Moderate CSME	No. of eyes	%
Mild NPDR	0	0
Moderate NPDR	2	2
Severe NPDR	20	20
Very severe NPDR	8	8
Early PDR	8	8
High Risk PDR	0	0
Total	38	38 %

7 new eyes at the end of the study developed CSME

No evidence of hole or cystoids changes occurred

15 eyes underwent argon laser photocoagulation and showed regression of edema.

TABLE 7

HYPERTENSION IN DIABETIC ESRD ON DIALYSIS

TOTAL NO. OF PATIENTS = 50

Age	No. of Patients	%
55- 60	8	16
61- 65	8	16
66- 70	4	8

Hypertension was presenting 40% of the study group -20 patients.

Age distribution showed 55 -60yrs group had 8 people, 61 -65 yrs group had 8 patients and 66-70 yrs group had 4 patients.

TABLE 8

INCIDIENCE OF HYPERTENSION RETINOPATHY

TOTAL NO. OF EYES = 100

	No. of Eyes	%
Grade I	8	8
Grade II	8	8
Grade III	4	4
Grade IV	0	0

Combined retinopathy was present in 20 Patients of the total.

Grade I & Grade II were the majority.

FUNDUS PICTURE OF KAMAYE –67/F – CASE- 47
(HPDR)

FUNDUS PICTURE OF KAMATCHI –68/F – CASE- 50
(HPDR)

TABLE 9

VISUAL ACUITY IN DIABETIC ESRD ON DIALYSIS

TOTAL NO OF EYES = 100

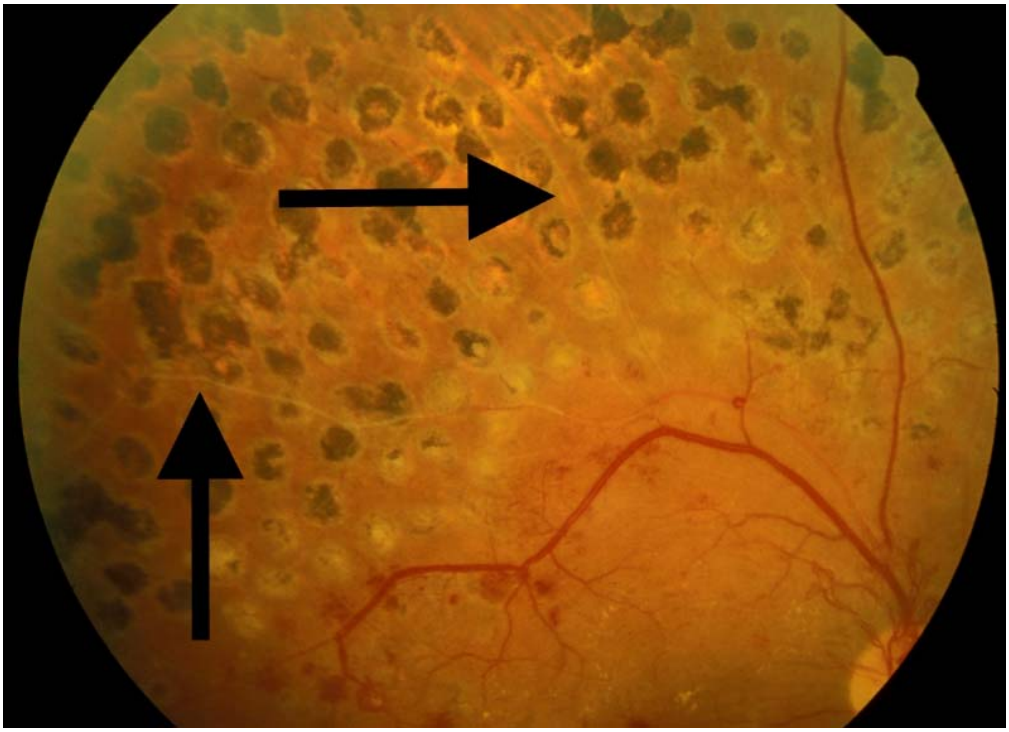
BCVA	Base line	Follow up
6/6	0	0
6/9	4	2
6/12	12	17
6/18	12	13
6/24	20	24
6/36	36	27
1/60 – 6/60	10	11
CfCf – HM	2	2
PL +_ PR	2	2
No PL	2	2

Visual acuity of no PL in two eyes was due to the presence of tractional retinal detachment majority of the visual acuity remained stable at the end of 6months. Few eyes showed progression of cataract.

Drop in visual acuity in three eyes was due to hard exudates near the macula.

15 eyes that underwent photocoagulation were found to improve in visual acuity of 1-2 line.

PAN RETINAL PHOTO COAGULATION OF KAMATCHI CASE- 50



DISCUSSION

This study was a nonrandomized prospective study including 50 patients with ESRD on dialysis of Diabetes mellitus origin conducted in a tertiary hospital in South India. Patients were referred from the department of nephrology for detailed opthalmological checkup. Renal failure was diagnosed with the criteria mentioned in patients and methodology. All patients underwent routine haemodialysis. Most of the patients due to reasons of inability to come for the ideal 3week schedule underwent 1 week dialysis schedule. No difference is tried to be made with respect to whether acetone or bicarbonate dialysis was done.

AGE DISTRIBUTION

The majority of the patients in the study were in the age group 55-60years accounting for about 60% of the total. In the study conducted by John et al (1989) it was found that patients developing nephropathy and renal failure with underlying NIDDM had early onset of disease between 30 and 50 years accounting for almost 75%. Brenner et al found age distribution of ESRD patients of diabetic origin to be higher at 56 years. Robert C Ramsamy et al group of patients on an average were 48 years but this study group included both type I type II DM.

SEX DISTRIBUTION

Males and females were studied for their distribution in relation to retinopathy and nephropathy. It was found that ESRD of diabetic origin showed a slight female preponderance accounting for about 56%. John et al in the Indian study at CMC, Vellore showed a striking male preponderance especially with early nephropathy. As nephropathy proceeds renal failure it was not possible to conclude if males were effected earlier in this study.

In the study conducted by Berman et al similar results were noted with females undergoing dialysis in upto 68% of the total. Robert C. Ramsamy et al showed almost equal distribution of males and females in their study. Three suppositions were given by Avram et al to explain why there are more women among the dialysed diabetic studied (1) women with diabetes mellitus live longer with the disease than men do. (2) women with diabetes may be more metabolically stable (3) More women are willing to accept dialysis and endure stress than are men.

CLASSIFICATION

Diabetic Retinopathy was graded under the ETDRS classification with hypertensive retinopathy graded under keith wagner Barker Classification. Berman et al followed a classification that combined both Kanski and ETDR classification. The retinopathy was classified as no

Retinopathy, background retinopathy macular edema, nonproliferative retinopathy + macular edema, proliferative retinopathy, vitreous hemorrhage and tractional retinal detachment. More simpler classification have also been followed like in the Jean-Louis Brenato Fenck study mentioned in Diabetic Renal – retinal syndrome as early, edematous, mixed, ischemic and complicated. People with hypertension were classified in 4 groups as common arteriosclerosis, cross sign, exudates and papilledema.

RETINOPATHY AND NEPHROPATHY

Frequency of retinopathy and nephropathy is explained in the WESDR study. An increasing frequency of retinopathy was found with increasing duration of diabetes. Prevalence rose sharply from 13.61% in those with diabetes of less than 5 years to 95.3%. In those with diabetes hypertension are present in all cases with significant proportion of people dying of uremia when there is associated underlying proliferative retinopathy.

In the Indian Study John et al (1989) it was found that out of 86% of people with diabetic retinopathy 20% of the people had proliferative changes. Whereas in this study the distribution of retinopathy was mild NPDR 0% moderate NPDR 8%, Severe NPDR 44% , very severe NPDR 24% early PDR 18% and high risk PDR 6%. This study was concordant with

Bermal et al which showed a high percentage of background retinopathy and non-proliferative retinopathy in their study in the range of 52%.

Robert C Ramsamy et al in the study conducted on insulin dependent diabetes ESRD patients found proliferative diabetic retinopathy to be common at 59% at the outset of dialysis. Studies conducted by Engrafov et al showed that main risk factor or risk of non proliferative retinopathy are the duration and degree of compensation of diabetes mellitus and stage of diabetic nephropathy. In this study the underlying nephropathy is severe needing medical and renal replacement therapy hence the presence of very severe, severe and proliferative retinopathy being common. To increase the specificity of renal insult and retinopathy Schwartz et al showed histological evidence of Kimmelstiel Wilson nodules and sever retinopathy. No renal biopsy was however done in any of our cases.

HYPERTENSION

Incidence of hypertension and associated retinoapathy was 40% in our group of study. Epidemological studies mention hypertension as a risk factor for the development of diabetic retinopathy and may be superimposed on diabetic retinopathy.

Yazdani et al study showed out of 64 patients with CRF, 21 had Diabetes and hypertension accounting to about 32%. In this study, most

common retinopathy graded was group 1& 2 of Keith wagner Barker classification. Hypertension could be the underlying risk factor for the development of severe retinopathy.

CSME

Clinically significant macular edema was noted in a significant proportion of patients at the out set of dialysis. It was noted to be 31%. The main visual morbidity in diabetes mellitus is CSME. The WESDR study noted significant also associations of proteinuria and macular edema was the commonest cause of visual morbidity in the Brener et al study.

VISUAL ACUITY

Robert C.Ramsay et al in their study conformed the stabilization of baseline visual acuity in a majority and deteroriation in some. Patients on dialysis in this study by Robert C.Ramsamy were both Type I and Type 11DM and followed for a minimum of 2 years on dialysis. As are study had a short follow up the end result could not be compared though similar causes of visual loss were found to be proliferative retinopathy and macular edema. Moreover where type 1 DM is associated with greater incidence of proliferative retinopathy on long term the same does not hold good for Type 11DM who formed the major in this study group.

Berman et al noted 7eyes in background retinopathy and 8eyes of non proliferative retinopathy to have macular edema. Both these groups constituted a majority of the total retinopathy. Prompt treatment in the form of focal, panretinal photocoagulation or both resulted in stabilization of vision. Whereas in out study photocoagulation was not included.

Deterioration in visual acuity in our study demonstrated coincident with CSME and in some to the appearance of hard exudates on macula. Kline et al has suggested that type II DM is a group prone to macular edema. Baseline visual acuity was noted to be stabilized in a majority but this was just a I year follow up which needs to be further followed up for long time.

15eyes underwent photocoagulation for macular edema and showed improvement at the end of six months in the form of improved visual activity of 1-2 lines.

Other patients with clinically significant macular edema were advised to undergo photocoagulation.

SUMMARY

End stage renal disease is a microvascular insult of diabetes where retinopathy is also common. In this study of 50patients all end stage renal disease patients had retinopathy as it was one of the inclusion criteria. Common retinopathy seen was severe, very severe NPDR and PDR.

All patients had NIDDM, in whom renal failure occurs after 5 years of the duration of the disease. Nephropathy is more common among IDDM but as the number of NDDM far exceeds the number of IDDM hence the total number of patients with ESRD is also greater. In India 5% of the diabetic population die of end stage renal disease.

Hypertension was seen in 40% of the study population. Whether it is the primary pathology or secondary result of ESRD is not known. Hypertension is by itself known to be associated with progression of non proliferative to proliferative retinopathy macular edema and retinopathy stabilization need good control of hypertension.

Majority of the patients were in the age group 55-60yrs with women accounting for the majority. Indian studies by John et al have showed earlier onset of nephropathy. The most common retinopathy seen was severe 44% and very severe NPDR 24%.

Progression of retinopathy was seen in minority of 4 eyes at the six months.

Macular edema was seen in 31 eyes at the onset of dialysis. Seven new eyes developed macular edema at the end of six month follow up.

Macular edema is a pathology that needs prompt treatment. 15% eyes that underwent photocoagulation showed 1-2 line improvement.

Better understanding of importance of control of hypertension, improvement in hemodynamic monitoring, increased accessibility of dialysis units have improved the quality of life of people on dialysis and provide an opportunity for timely opthalmological intervention.

With majority of the studies having shown raised blood pressure poor glycaemic control and renal insufficiency as association of severe retinopathy, treatment with prompt opthalmogical intervention in the form of photocoagulation or vitrectomy decrease the visual impairment.

CONCLUSION

- End stage renal disease of NIDDM is always associated with retinopathy as both are microvascular damage of the same disease of the same disease process.
- Severe NPDR is the most common retinopathy.
- Hypertension occurs in 40% of ESRD patients of NIDDM.
- Combined retinopathy accounts for about 40% of the retinopathy.
- Patients between 55-60yrs who are known to be diabetic are commonly associated with ESRD and retinopathy.
- ESRD is found to be commonly associated with females.
- Macular edema is seen in 31% of the patients with retinopathy.
- Macular edema stabilizes with control of hypertension and dialysis.
- New eyes without macular edema could however also develop macular edema during hemodialysis.
- Diabetic retinopathy stabilizes on a short term basis in people with ESRD on dialysis.
- Few eyes could progress in retinopathy when even on dialysis.

- Macular edema accounts for a subset of visual morbidity.
- Prompt treatment in the form of photocoagulation and vitrectomy is utomost importance to reduce the visual impairment and improve quality of life.
- It is also important for patients with diabetic ESRD to undergo opthalmological evaluation regularly.
- Conditions that may affect the course of diabetic retinopathy like hypertension, elevated triglycerides, protein urea & cardiovascular disease should be look for and kept under control.

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PROFORMA

Name Age Sex

Mrd.No.

Diagnosis

History of Diabetes Mellitus - Duration

Hypertension - Duration

Renal Parameters BUN

Creatinine

Treatment History

Haemodialysis Frequency

Type of Dialysis

Duration

Ophthalmological evaluation. RE LE

Best corrected visual acuity.

Anterior segment evaluation.

Lids

EOM

Pupil

Lens

Slit lamp biomicroscopy with 90D

Fundus Direct Opthalmoscopy

Fundus Indirect Opthalmoscopy

Fundus photographs

Fundus flourescein angiography

Grading of retinopathy

Follow up Repetition of above six months and one year.

MASTER CHART

S. NO	Name	Age	Sex	OP.No	H/o DM Yrs	H/o DM Yrs	V/A"0" Months		Retinopathy "0" Months		V/A"0" Months		Retinopathy "6" Months	
							RE	LE	RE	LE	RE	LE	RE	LE
1	Jeyaraman	55	M	470121	7		6/9	6/9	Mod NPDR+ CSME	Mod NPDR + CSME	6/9	6/18	Mod NPDR+ CSME	Mod NPDR + CSME
2	Muthuraman	55	M	471341	8	7	6/12	6/12	Mod NPDR+ CSME+ GrIHTR	Mod NPDR+ CSME+ GrIHTR	6/9	6/18	Mod NPDR+ CSME+ GrIHTR	Mod NPDR+ CSME+ GrIHTR
3	Lakshmanan	56	M	471432	12	8	6/12	6/12	Mod NPDR+ GrIHTR	Mod NPDR+ GrIHTR	6/12	6/12	Mod NPDR+ GrIHTR	Mod NPDR+ GrIHTR
4	Chinnaswamy	57	M	471741	13	10	6/12	6/12	Mod NPDR+ GrIHTR	Mod NPDR+ GrIHTR	6/12	6/12	Mod NPDR+ GrIHTR	Mod NPDR+ GrIHTR
5	Jegan	57	M	471934	11	8	6/12	6/12	SNPDR+ GrIHTR	SNPDR+ GrIHTR	6/12	6/12	SNPDR+ GrIHTR	SNPDR+ GrIHTR
6	Lakshmanan	56	M	482130	12	10	6/12	6/12	SNPDR+ GrIHTR	SNPDR+ GrIHTR	6/12	6/12	SNPDR+ GrIHTR	SNPDR+ GrIHTR
7	Rajesh	58	M	482242	9	6	6/12	6/12	SNPDR+ CSME- GrIHTR	SNPDR+ CSME+ GrIHTR	6/12	6/12	SNPDR+ CSME+ GrIHTR	SNPDR+ CSME+ GrIHTR
8	Ramaiah	59	M	482450	8	7	6/12	6/12	SNPDR+ CSME+ GrIHTR	SNPDR+ CSME+ GrIHTR	6/12	6/12	SNPDR+ CSME+ GrIHTR	SNPDR+ CSME+ GrIHTR
9	Ramesh	59	M	482452	11	5	6/36	6/36	SNPDR+ CSME	SNPDR+ CSME	6/12	6/12	SNPDR+ CSME	SNPDR+ CSME

10	Suresh	59	M	484350	11		6/36	6/36	SNPDR+ CSME	SNPDR+ CSME	6/12	6/12	SNPDR	SNPDR+ CSME
11	Selvaraj	60	M	484431	10		6/36	6/36	SNPDR+ CSME	SNPDR+ CSME	6/12	6/18	SNPDR	SNPDR+ CSME
12	Ganesh	60	M	484521	10		6/36	6/36	SNPDR+ CSME	SNPDR+ CSME	6/18	6/18	SNPDR	SNPDR+ CSME
13	Vasan	60	M	484630	11		6/36	6/36	SNPDR+ CSME	SNPDR+ CSME	6/18	6/18	SNPDR+ CSME	SNPDR+ CSME
14	Pandian	60	M	484680	11	9	6/36	6/36	SNPDR+ CSME	SNPDR+ CSME	6/18	6/18	SNPDR+ CSME	SNPDR+ CSME
15	Seetha	56	F	484757	12	9	6/24	6/24	SNPDR+ GrIHTR	SNPDR+ GrIHTR	6/24	6/24	SNPDR+ GrIHTR	SNPDR+ GrIHTR
16	Ambika	57	F	484850	12	3	6/24	6/24	SNPDR+ GrIHTR	SNPDR+ GrIHTR	6/24	6/24	SNPDR+ GrIHTR	SNPDR+ GrIHTR
17	Alamelu	58	F	484900	13	4	6/24	6/24	SNPDR+ GrIHTR	SNPDR+ GrIHTR	6/24	6/24	SNPDR+ CSME+ GrIIHTR	SNPDR+ CSME+ GrIIHTR
18	Rajammal	58	F	484971	13	7	6/24	6/24	SNPDR+ GrIHTR	SNPDR+ GrIHTR	HM	HM	SNPDR+ CSME+ GrIIHTR	SNPDR+ CSME+ GrIIHTR
19	Sumathi	59	F	484980	12		6/24	6/24	SNPDR	SNPDR	6/24	6/24	SNPDR+ CSME+ GrIIHTR	SNPDR+ CSME+ GrIIHTR
20	Laksmi	58	F	490000	12		6/24	6/24	SNPDR	SNPDR	6/24	6/24	SNPDR+ CSME	SNPDR
21	Muthu	59	M	491321	11		6/12	6/12	SNPDR	SNPDR	6/18	6/18	SNPDR	SNPDR
22	Somu	59	M	491334	11		6/12	6/12	SNPDR	SNPDR	6/18	6/18	SNPDR	SNPDR

23	Veeralakshmi	58	F	494231	12		6/24	6/24	SNPDR	SNPDR	6/24	6/24	SNPDR	SNPDR
24	Karpagam	57	F	494421	12		6/24	6/24	SNPDR	SNPDR	6/24	6/24	SNPDR	SNPDR
25	Kumari	60	F	494700	15		6/36	6/36	SNPDR	SNPDR	6/36	6/36	SNPDR	SNPDR
26	Velammal	59	F	495200	15		6/36	6/36	SNPDR	SNPDR	6/36	6/36	SNPDR	SNPDR
27	Radhika	55	F	496111	14		6/36	6/36	VSNPDR+ CSME	VSNPDR	6/36	6/36	VSNPDR	VSNPDR
28	Sundari	57	F		13		6/36	6/36	VSNPDR+ CSME	VSNPDR	6/36	6/36	VSNPDR	VSNPDR
29	Kathayee	56	F	496321	12		6/36	6/36	VSNPDR	VSNPDR	6/36	6/36	VSNPDR	VSNPDR
30	Ramaselvi	56	F	496421	12		6/36	6/36	VSNPDR	VSNPDR	6/36	6/60	VSNPDR	VSNPDR
31	Keerthi	62	M	496520	12	8	6/36	6/36	VSNPDR+ CSME GrIIHTR	VSNPDR+ CSME GrIIHTR	6/36	6/60	VSNPDR+ GrIIHTR	VSNPDR+ GrIIHTR
32	Kumaran	63	M	497324	12	7	6/18	6/18	VSNPDR+ CSME GrIIHTR	VSNPDR+ CSME GrIIHTR	6/36	5/60	VSNPDR+ GrIIHTR	VSNPDR+ GrIIHTR
33	Veilvandan	62	F	497338	12		6/18	6/18	VSNPDR	VSNPDR	2/60	6/18	VSNPDR	VSNPDR
34	Kannammal	62	F	497426	12		6/18	6/18	VSNPDR	VSNPDR	6/18	6/18	VSNPDR	VSNPDR
35	Laksnmi	62	F	497440	16		6/18	6/18	VSNPDR+ GrIIHTR	VSNPDR+ GrIIHTR	6/12	6/18	VSNPDR+ GrIIHTR	VSNPDR+ GrIIHTR
36	Periammal	62	F	497523	16	6	6/36	6/36	VSNPDR+ GrIIHTR	VSNPDR+ GrIIHTR	6/24	6/24	VSNPDR+ GrIIHTR	VSNPDR+ GrIIHTR
37	Perumaye	65	F	497538	16	8	6/36	6/36	VSNPDR+ GrIIHTR	VSNPDR+ GrIIHTR	6/36	5/60	VSNPDR+ GrIIHTR	VSNPDR+ GrIIHTR

38	Subbu	65	F	498420	16	5	6/36	6/36	VSNPDR+ GrIIHTR	VSNPDR+ GrIIHTR	5/60	5/60	VSNPDR+ GrIIHTR	VSNPDR+ GrIIHTR
39	Petchi	61	F	499804	17	3	6/36	6/36	EPDR+ GrIIHTR	VSNPDR+ GrIIHTR	6/24	6/24	EPDR+ GrIIHTR	VSNPDR+ GrIIHTR
40	Chandra	62	F	499916	17	6	6/36	6/36	EPDR+ CSME	VSNPDR+ GrIIHTR	6/24	6/24	EPDR+ CSME	VSNPDR+ GrIIHTR
41	Lakshmi	66	M	503424	17	8	6/36	6/36	EPDR+ CSME	EPDR+ CSME	6/24	6/24	EPDR+ CSME	EPDR+ CSME
42	Sundaram	67	M	513632	17	9	1/60	5/60	EPDR+ CSME	EPDR+ CSME	HM	5/60	EPDR+ CSME	EPDR+ CSME
43	Veerasamy	67	M	513754	17	10	5/60	2/60	EPDR+ CSME	EPDR+ CSME	5/60	HM	EPDR+ CSME	EPDR+ CSME
44	Sundaram	67	M	516432	17	8	6/36	6/36	EPDR	VSNPDR	6/36	6/36	EPDR	VSNPDR
45	Meenakshi	66	F	527436	17	8	1/60	3/60	HPDR	EPDR	1/60	3/60	HPDR	EPDR
46	Raasathi	67	F	538327	16		1/60	3/60	HPDR	EPDR	1/60	3/60	HPDR	EPDR
47	Kamaye	67	F	549438	16		2/60	Cfcf	HPDR	EPDR	2/60	Cfcf	HPDR	EPDR
48	Saraswathi	67	F	553674	16		2/60	Cfcf	HPDR	HPDR	2/60	Cfcf	HPDR	HPDR
49	Revathi	67	F	564384	20		Nopl	Pl+Pr	HPDR	HPDR	NOP1	Pl+Pr	HPDR	HPDR
50	Kamatchi	68	F	583842	21		Pl+PR	Nopl	HPDR	HPDR	Pl+PR	Nopl	HPDR	HPDR

MASTER CHART KEY

DM- Diabetes Mellitus

HT-Hyper tension

Yrs - Years

RE-Right Eye

LE- Left Eye

V/A - Visual acuity

S- Severe

HR - high risk

NPDR - non proliferatvie diabetic retinopathy

PDR - proiferative diabetic retinopathy

PL - perception of light

Mod - moderate

VS - very severe

E - early

PR - projection of ray of light

HM - hand movement